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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,088	12/05/2003	Martinus Bernardus Vrouenracts	2344-40	8108

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,088	VROUENRAETS ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) 5-12 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Vrpiemraets et al.

DETAILED ACTION

Application Status

Claims 1-12 are currently pending and under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 9/17/2002 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claims 5-12 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Latouche et al. (Tetrahedron Letters 1995: 36: 1664-1666, IDS).

Latouche et al. disclose a porphyrin derivative lacking an antibody which appears to 100% identical to the instantly claimed ring structure of formula (VIII), wherein the ring is a porphyrin ring carrying four aromatic phenyl substituted Ar's carrying one or more hydroxyl groups suitably linked via a ether linkage to a carboxyl group (compound shown on page 1665).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Latouche et al. (Tetrahedron Letters 1995; 36: 1664-1666, IDS) in combination with Mauclaire et al. (US Patent 5,268,371, 1993).

Latouche et al. disclose, as applied to claim 4 above, a porphyrin derivative lacking an antibody which appears to 100% identical to the instantly claimed ring structure of formula (VIII), wherein the ring is a porphyrin ring having four aromatic phenyl substituted Ar's carrying one or more hydroxyl groups suitably linked via a ether linkage to a carboxyl group, e.g., COOH (compound shown on page 1665). The reference further teaches (page 1665, 1st paragraph, lines 3-5) that radiolabelled mealloporphyrins have significantly improved the efficacy of porphyrins for tumor detection, wherein the method can be improved by associating a radioactive metal complex and an antibody in order to deliver the reagent to a specific target. Moreover, Latouche et al. teach that the specific insertion of the metal in the porphyrin even in the presence of a good copper chelator like bovine albumin allows preliminary coupling of these ortho substituted porphyrins with antibodies before ^{64}Cu insertion (page 1666, lines 13-15).

Latouche et al. does not explicitly teach that the porphyrin derivative having four aromatic phenyl substituted Ar's carrying one or more hydroxyl groups is in turn linked via the COOH group to an antibody directed against a cell surface antigen of cancer or other diseased cells.

Mauclaire et al. teach derivatives of porphyrins and metalloporphyrins conjugated to a biologically active molecule (Title). With regards to the biologically active molecule, the patent

teaches (column 8, lines 66-68 and column 9, lines 33-34) that such biologically active molecules include, but are limited to, antibodies, wherein the antibodies are directed against a cell surface antigen of the cancer cells. Specifically, Mauclaire et al. teach (column 5, lines 38-53) that the presence of the COOH group on the porphyrin gives them the property of being covalently bondable to biologically active molecules such as antibodies.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Latouche et al. and Mauclaire et al.. One would have been motivated to do so because as taught by both Latouche et al. and Mauclaire et al., porphyrin derivatives coupled to a biologically active molecule have a better affinity due to the presence of said biologically active molecule, e.g. target cell specificity (page 1665, 1st paragraph, lines 3-5 and column 9, lines 28-34 respectively). Thus, one of ordinary skill in the art would have a reasonable expectation that by conjugating an antibody with a porphyrin derivative as taught by Latouche et al. in view of Mauclaire et al., one would achieve a cancer cell specific porphyrin antibody conjugate which may be used for detection and/or treatment of tumor cells.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonnet et al. (US Patent 4,992,257, 1991, IDS) in combination with Latouche et al. (Tetrahedron Letters 1995; 36: 1664-1666, IDS) and Mauclaire et al. (US Patent 5,268,371, 1993) in view of Westerman et al. (Int. J. Cancer 1998; 76: 842-850).

Bonnet et al. teach (column 8, lines 37-68) dihydro and tetra-hydro porphyrins (referred to as chlorins and bacteriochlorins respectively, column 6, lines 21-24) having four aromatic phenyl substituted rings carrying one or more hydroxyl groups, wherein the hydroxyl groups may be in the ortho, para or meta position. With regards to the dihydro and tetra-hydro porphyrins, the patent teaches that the dihydro and tetra-hyrdro porphyrins include, but are not limited to, p-THPC, m-THPC, o-THPC and m-THPBC (column 6, Table 2). Bonnet et al. further teach (column 1, line 65 to column 2, line 1) that the compounds can be used as a form of cancer therapy, wherein the compound is administered to locate in the tumor followed by illumination of the tumor with light of a wavelength absorbed by the compound.

Bonnet et al. do not explicitly teach that the dihydro and tetra-hydro porphyrins (referred to as chlorines and bacteriochlorins respectively, column 6, lines 21-24) having four aromatic phenyl

substituted rings carrying one or more hydroxyl groups are in turn linked to an antibody against a cell surface antigen of cancer cells. Nor does Bonnet et al. teach that the antibody and porphyrin derivatives are linked via an ether linkage through a COOH group.

The combination of Latouche et al. and Mauclaire et al. teach, as applied to claims 1 and 3-4 above, a porphyrin derivative having four aromatic phenyl substituted Ar's carrying one or more hydroxyl groups linked via a ether carboxyl group, e.g., COOH, to an antibody which binds a surface cell cancer antigen. Moreover, Mauclaire et al. teach (column 5, lines 38-53) that the presence of the COOH group on the porphyrin gives them the property of being covalently bondable to biologically active molecules such as antibodies, while Latouche et al. teach a method of generating the porphyrin derivative having an ether linked COOH group via alkylation of the phenolic hydroxyl by ethyl bromoacetate followed by saponification of the ester group (page 1665, last paragraph).

Westermann et al. teach (page 842, 2nd column, 1st full paragraph) that the major disadvantages of m-THPC phototherapy include, but are limited to, a relatively low tumor selectivity which, in view of the strong photoxic properties, can lead to undesired side effects in adjacent normal tissues. As a way to circumvent this disadvantage, the reference teaches a conjugate comprising the photosensitizer metal-tetrahydroxyphenylchlorin (m-THPC) conjugated to polyethylene glycol which preserves its function of phototherapy and represents an interesting first step in favor of the strategy of conjugating photosensitizing dyes to anti-tumor antibodies (page 849, 2nd column, 2nd paragraph).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to specifically target a cancer cell with m-THPC. One would have been motivated to do so because as taught by Westerman et al., one of the major disadvantages with m-THPC phototherapy is the lower tumor selectivity that leads to undesirable side effects. Thus, one of ordinary skill in the art would have a reasonable expectation that by alkylating the hydroxyl groups of m-THPC followed by saponification in view of Latouche et al., one would achieve a covalently bondable COOH group on m-THPC which can be linked to an antibody for specific tumor localization of m-THPC.

Moreover, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established

scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983).

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
12/5/05